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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,029	01/17/2007	Gerwyn Bish	PC32050A	1793

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PATENT DEPARTMENT
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EXAMINER	
LEESER, ERICH A	
ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
08/10/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~IPGSGro@pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	10/586,029	BISH ET AL.	
	Examiner	Art Unit	
	Erich A. Leeser	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *24 and 25* is/are allowed.

6)☒ Claim(s) *26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to Applicant's submission dated March 19, 2009, in which Applicant cancelled claims 1-23 and added new claims 24-30.

Claim Rejections - 35 USC § 102

Examiner previously rejected claims 1, 3-9 and 11-12 under 35 USC 102(b) as being anticipated by Natsuka, et al., *Synthesis and Structure-Activity Relationships of 1-Substituted 4-(1,2-Diphenylethyl)piperazine Derivatives Having Narcotic Agonist and Antagonist Activity*, Journal of Medicinal Chemistry, Vol. 30, 1779-87 (1987).

Based on Applicant's cancellation of the rejected claims, Examiner withdraws this rejection.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because while the specification is enabled with regard to the treatment of pain, the specification does not enable the instant compounds to treat a disorder in which the regulation of serotonin or noradrenaline is implicated; urinary disorders, depression, premature ejaculation, ADHD or fibromyalgia; urinary incontinence; genuine stress incontinence

or stress urinary incontinence using an effective amount of a compound corresponding to claim 24 or enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention:

The instant invention is drawn to (+) or (-)-1-[2-(2-ethoxyphenyl)-1-phenylethyl]piperazine, a composition containing same and various methods which allegedly purport that the invention is useful to treat a disorder in which the regulation of serotonin or noradrenaline is implicated; urinary disorders, depression, premature ejaculation, ADHD or fibromyalgia; urinary incontinence; genuine stress incontinence or stress urinary incontinence using an effective amount of a compound corresponding to claim 24.

The state of the prior art:

The prior art at the time the invention was made tends to show the lack of understanding in the synthetic organic chemistry community as to the use, function, and relevant activity of serotonin and noradrenaline re-uptake inhibitors regarding the treatment of urinary incontinence:

"Stress urinary incontinence (SUI) is the accidental leakage of urine associated with physical activities such as running, jumping or lifting or with sneezing and coughing. For many patients it can be a very bothersome symptom, causing social isolation, loss of self-esteem and increased financial outlays. Although *there is currently no medication approved worldwide for the treatment of SUI*, a variety of off-label agents are sometimes prescribed. Duloxetine (LY-248686; Eli Lilly), a new centrally acting compound with dual activity as a serotonin and noradrenaline re-uptake inhibitor, offers a *promising* new approach for treatment. Due to its inhibition of presynaptic neuron re-uptake of serotonin and noradrenaline in the sacral spinal cord, duloxetine is *believed* to increase the strength of urethral sphincter contractions and thereby prevent accidental urine leakage by increasing urethral closure pressure." (Emphasis added). Zinner, *Duloxetine: A Serotonin-noradrenaline Re-uptake Inhibitor for the Treatment of Stress Urinary Incontinence*, Expert Opinion on Investigational Drugs, Vol. 12, No. 9, pp. 1559-66 (2003 Sep).

The predictability in the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the claimed invention is highly unpredictable since one skilled in the art would not necessarily recognize, with regards to therapeutic effects, whether or not the compound of claim 24 would be useful to treat treat a disorder in which the regulation of serotonin or noradrenaline is implicated; urinary disorders,

depression, premature ejaculation, ADHD or fibromyalgia; urinary incontinence; genuine stress incontinence or stress urinary incontinence.

Amount of guidance/working examples:

Beginning on page 58 Applicant provides a section of the specification entitled "Biological Activity" ending on page 60 with Table 1. These examples in the specification; however, do not definitively prove that the instant compound can be used to effectively treat a disorder in which the regulation of serotonin or noradrenaline is implicated; urinary disorders, depression, premature ejaculation, ADHD or fibromyalgia; urinary incontinence; genuine stress incontinence or stress urinary incontinence using an effective amount of a compound corresponding to claim 24.

The breadth of the claims:

The breadth of claims in claims 26-27 are overly broad as they do not recite specific diseases or disorders, but simply classes of diseases or disorders generally; i.e., "a disorder in which the regulation of serotonin or noradrenaline is implicated; urinary disorders". Claims 29-30 are not unduly broad as it is limited to the specific disorders: "depression, pain, premature ejaculation, ADHD or fibromyalgia; urinary incontinence; genuine stress incontinence or stress urinary incontinence".

The quantity of undue experimentation needed:

Since the guidance and teaching provided by the specification is insufficient to treat a disorder in which the regulation of serotonin or noradrenaline is implicated; urinary disorders, depression, premature ejaculation, ADHD or fibromyalgia; urinary incontinence; genuine stress incontinence or stress urinary incontinence with an effective amount of a compound of claim 24,

one of ordinary skill in the art, even with a high level of skill, is unable to use the instant compounds to treat a disorder in which the regulation of serotonin or noradrenaline is implicated; urinary disorders, depression, premature ejaculation, ADHD or fibromyalgia; urinary incontinence; genuine stress incontinence or stress urinary incontinence as claimed without undue experimentation.

The level of the skill in the art:

The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art; however, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which diseases or diseases would benefit from this activity.

Taking all of the above factors into consideration, it is not seen how one of ordinary skill in the art would be able to make and use the compounds of claim 24 to treat a disorder in which the regulation of serotonin or noradrenaline is implicated; urinary disorders, depression, premature ejaculation, ADHD or fibromyalgia; urinary incontinence; genuine stress incontinence or stress urinary incontinence without undue experimentation.

Allowable Subject Matter

Claims 24-25 are patentable over compounds 19 and 20 of Natsuka, et al., *Synthesis and Structure-Activity Relationships of 1-Substituted 4-(1,2-Diphenylethyl)piperazine Derivatives Having Narcotic Agonist and Antagonist Activity*, Journal of Medicinal Chemistry, Vol. 30, 1779-87 (1987). There are two differences between compounds 19 and 20 of the reference and the instant compound and composition. First, X of the reference teaches methoxy instead of

ethoxy. Second, X of compounds 19 and 20 of the reference is a positional isomer of the ethoxy substituent of the instant compound and composition. Therefore, the claims are free of prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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